HERPES SIMPLEX VIRUS TYPE 1 IN BRAIN: AN ENVIRONMENTAL RISK FACTOR IN ALZHEIMER'S DISEASE

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The causes of sporadic Alzheimer's disease (AD) are unknown although possession of one or both alleles of the E4 variant of the gene for apolipoprotein E (ApoE4) is a strong risk factor for the disease. However, not all ApoE4 heterozygotes or even homozygotes develop AD, and not all AD patients carry even one E4 allele. Presumably, therefore, environmental as well as genetic factors play a role. One possible environmental factor is a virus - a number of rare neurological disorders are known to be caused by common viruses - and in particular, herpes simplex virus type 1 (HSV1): this virus is ubiquitous, it has a predilection for latent residence in the peripheral nervous system, and it targets, in acute HSV1 encephalitis, the same CNS regions - temporal and/or frontal cortex and/or hippocampus - as those most affected in AD. In these regions, using polymerase chain reaction (PCR) (and taking stringent precautions against artefacts) we have detected latent HSV1 in post mortem brain from about 2/3 of both aged normals and AD patients; in the occipital cortex, a much less affected region, we have found no viral DNA. We have now examined the ApoE genotype of 26 AD cases and 26 aged normals. We have found that the odds ratio with 95% confidence intervals for the ApoE4 allele for HSV1-positive ADs /HSV1 positive normals is significantly higher than for total ADs /total normals, i.e., for ApoE4 alone. Our results suggest that the risk of developing AD is greater for ApoE4 heterozygotes and homozygotes who have HSV1 DNA in one or more specific regions of their CNS than for those possessing an E4 allele but who are HSV1-negative in these regions.